Scientific Abstract

Interleukin-12 (IL-12) is a heterodimeric cytokine which has potent anti-tumor effect in mouse tumor models suppressing tumor growth when administered systemically or locally using fibroblasts genetically modified to produce IL-12. In preclinical mouse tumor models, induction of long term tumor immunity was variable in a systemic administration model but significant immune protection is observed when irradiated tumor cells are administered mixed with fibroblasts genetically engineered to secrete IL-12 . Furthermore, injection of fibroblasts infected with a retroviral vector expressing IL-12 can eradicate the well established day 7 tumors in animal models. This form of IL-12 administration, when appropriately modified, appears suitable for a clinical trial.

This clinical trial will include patients in Korea with disseminated cancers who have accessible subcutaneous tumor(s). The toxicities and feasibility of this treatment will be evaluated as primary objectives of this protocol. Efficacy and immunomodulatory effect of this treatment will be examined on both the local tumor or uninjected tumors at other sites if possible.

Before beginning treatment, physician will perform a history and physical examination. The patient will have blood tests, a urinalysis, a chest x-ray, an electrocardiogram, and CT or MRI scans performed. Blood will be drawn on days 0 (pre-treatment), 7, 14, 21, 28, 35, and 42.

In order to perform this study, fibroblasts will be prepared from a piece of the individual patient's skin (½ inch wide and 2 inches long). Fibroblasts will be placed in culture, propagated, transduced with the retroviral vector termed TFG-hIL-12-Neo which carries interleukin-12 (IL-12) genes and Neo gene. After the transduction, the cell will be selected by G418, further propagated, tested for IL-12 expression in culture, harvested, irradiated, and then injected into the

tumor lesions of the patient. These sites will be marked with permanent india ink. The patient is required to return to the clinic next day of these injections for the purpose of evaluating me for any side effects.

One week after the first injection, the patient will receive the same procedure except injecting the fibroblasts NOT secreting interleukin-12 after the evaluation of first injection. Twenty eight days after the first injections, two injection sites will be biopsied under local anesthesia. Lastly, the patients are required to return to the clinic one and two months after the last injections to evaluate the progress.